

**CLAIM REJECTIONS 35 U.S.C. 102(b)**

All seven claims pending have been rejected under 35 U.S.C. 102(b) as being anticipated by Johansson et al.; Taylor et al.; or Yeung et al. However, as discussed below, none of the prior art apparatus is for carrying out whole column imaging detection (WCID) for capillary isoelectric focusing (CIEF).

Independent claim 1 and, by importation, dependent claims 2-7 of this application are directed to apparatus “for capillary isoelectric focusing”, including “whole column imaging detection means for monitoring the isoelectric focusing process”. In the summary of claim 1 tabulated at page 3 of his Action, the Examiner has identified component (c) only as “column imaging detection means for monitoring the isoelectric focusing process” and not whole column imaging detection means. That most critical limitation is not disclosed in any of the three references in issue.

**Johansson et al.**

Figure 1, at page 2234, clearly shows that in the experimental setup used by Johansson et al., the whole column was not imaged, only the last portion of the column. In the section entitled “2.3 Capillary electrophoresis”, it is indicated that Johansson et al.’s homemade electrophoresis system used uncoated fused-silica capillaries. It is well known in the art that the refractive index of fused-silica is very much greater than that of water, so that total internal reflection could not occur in this arrangement. That is to say, the Johansson et al. separation capillary is not “made of a material having a sufficiently low refractive index that the intensity of laser light scattered from the walls of said separation capillary is negligible relative to the fluorescence of the analytes in the migration medium”, as specified in the claims of this application.

Turning to Figure 4(a) at page 2236 of Johansson et al., the plot of intensity against capillary length shows that light intensity decayed exponentially along the capillary from the point of entry of the light. Consequently, light scattering was much greater near the point of entry. With such an optical arrangement, excitation light could not proceed to the other end of the capillary through multiple reflections at the water/capillary wall interface. It is for that reason that only the portion close to the end of the capillary was imaged by Johansson et al.

By contrast, in paragraph [007] of the present specification, an example is given of whole column imaging detection in which “the focusing process in 3 cm of a 5 cm separation capillary could be monitored”.

**Taylor et al.**

In the apparatus used by Taylor et al. for axial-beam laser-excited fluorescence detection in capillary electrophoresis, a fused-silica capillary was used, with DMSO added in the buffer to increase the refractive index of the electrolyte. Nevertheless, as seen in Figure 1 at page 1742, the absorbed fluorescence is from a confined (one-point) region about 1 mm removed from the end of the fiber. The detection of that fluorescence by a second optical fiber also clearly indicates that Taylor et al. is using “single point on-column” detection, as noted in the present specification, paragraph [0015].

Figure 5 at page 1744 of Taylor et al. presents an image about scattering centers inside a capillary, the image length being only about 0.5 mm – entirely unlike the present applicants’ whole column imaging detection method.

**Yeung et al.**

As with the apparatus of the two other cited references, the detector system arrangement disclosed and described in the Yeung et al. patent images only a small part of the capillary, clearly shown in Fig. 1 of U.S. Patent 5,324,401. Figures 2 and 3 show fluorescence imaging detection of multiplexed capillaries and not whole column images of a single capillary.

**CIEF contrasted with CIE**

In fact, not one of the cited references refers to capillary isoelectric focusing (CIEf) as its intended application but, rather, capillary zone electrophoresis (CZE). To use whole column imaging detection for capillary zone electrophoresis would afford none of the significant found discovered by the present inventors in experimenting with the use of WCID for CIEF. In CZE, the analyte zones are moving towards the detector, so there is no requirement to view them at every position along the capillary. For CIEF, however, the analytes are focused at positions corresponding to their respective isoelectric points. If a single detection point were used, then the zones would have to be mobilized, requiring an additional step and contributing to zone broadening.


Capillaries used in CZE are typically of considerable length to achieve sufficient resolution, so that it would not be possible to image the whole capillary. For example, Taylor et al. (page 1741, Experimental Section, 8<sup>th</sup> line from the bottom) specifies a 30 cm capillary of 75 micrometer inner diameter. Similarly, at page 2234, section 2.3, line 10 of Johansson et al., a 30 cm capillary having 100 micrometer inner diameter is called for. Yeung et al, in Example 1, specifies a capillary 27 cm long with an inner diameter of 75 microns and mentions that the same type of capillaries were used in Examples 2 and 3. There is no description in any of the prior art of imaging all or most of the whole 27-30 cm of length of capillary of such

small diameter.

Favourable reconsideration of claims 1-7 is therefore respectfully requested, on the bases that (1) none of the prior art apparatus shown to be "for capillary isoelectric focussing" (capillary zone electrophoresis) and (2) none incorporates "whole column" imaging detection means, as described and claimed in this application.

Respectfully Submitted,

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